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Dec 1, 1998

DOCUMENT-IDENTIFIER: US 5843669 A

TITLE: Cleavage of nucleic acid acid using thermostable methoanococcus jannaschii
FEN-1 endonucleasesDetailed Description Text (902):

Resistance to either or both of the antibiotics rifampin (rif) and isoniazid (inh) is the standard by which *M. tuberculosis* strains are judged to be multi-drug resistant. Both because of their potent bactericidal activities and because acquisition of primary resistance to these drugs is rare (the spontaneous mutation rate of resistance to rifampin is approximately 10.^{sup.-8} and to isoniazid, 10.^{sup.-8} to 10.^{sup.-9}), until very recently, these two antibiotics were among the most powerful front-line drugs used to combat the advance and spread of tuberculosis. However surveys of tuberculosis patients in the U.S. reveal that as many as one-third were infected with strains resistant to one or more antituberculosis drugs; greater than 25% of the *M. tuberculosis* cultures isolated were resistant to isoniazid and 19% were resistant to both isoniazid and rifampin [Frieden et al., *New Eng. J. Med.* 328:521 (1993)].

Detailed Description Text (1095):

From the above it is clear that the invention provides reagents and methods to permit the rapid screening of nucleic acid sequences for variations. These methods allow the identification of viral and bacterial pathogens as well as permit the detection of mutations associated with gene sequences (e.g., mutations associated with multiple drug resistance in *M. tuberculosis* or mutations associated with human disease). These methods provide improved means for the identification and characterization of pathogens.

Other Reference Publication (65):

Morris, et al., "Molecular Mechanisms of Multiple Drug Resistance in Clinical Isolates of *Mycobacterium tuberculosis*," *J. Infect. Dis.* 171:954-960 (1995).

Other Reference Publication (114):

Zwickl et al., "Glyceraldehyde-3-Phosphate Dehydrogenase from the Hyperthermophilic *Archaeabacterium Pyrococcus woesil*: Eharacterization of the Enzyme, Eloning and Sequencing of the Gene, and Expression in *Escherichia coli*," *J. Bacter.* 172:4329-4338 (1990).